

Remarks

Claims 1-18 were pending in the subject application. By this Amendment, claims 1, 9, 11, 12, and 16 have been amended, and new claim 19 has been added. Support for the amendments and new claim can be found throughout the subject specification including, for example, at page 1, lines 19-31, and page 3, lines 18-29. Applicants respectfully submit that no new matter is introduced by the amendments presented herein. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-18 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

Claims 1-18 are rejected under 35 USC §112, second paragraph, as indefinite. Applicants respectfully assert that the claims are clear and definite. However, by this Amendment, Applicants have amended claim 1 to lend greater clarity to the claimed invention. Claim 1 affirmatively recites each component of the respective heeled primers. Reference to “the FAP” and to “the primer sequences FAP and TAP” have been deleted from the claims; thus, the rejection for lack of antecedent basis is moot. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-6 and 8-18 are rejected under 35 USC §102(b) as anticipated by Richardson *et al.* (WO 01/06004 A2). In addition, claim 7 is rejected under 35 USC §103(a) as obvious over Richardson *et al.* in view of Fend *et al.* (1999). The Examiner’s assertion as to the teachings of the Richardson *et al.* publication is set forth at pages 3-7 of the instant Office Action. Applicants respectfully traverse these grounds of rejection.

Applicants respectfully assert that the cited references do not teach or suggest the claimed invention. The methods disclosed in the Richardson *et al.* publication require essentially **three steps**, *i.e.*, 1) reverse transcription of the mRNA species using a first heeled primer population, to provide first cDNA strands; 2) synthesis of second cDNA strands from the first, using a second heeled primer population; and 3) amplification of the first and second cDNA strands. By contrast, in the present invention, reverse transcription and production of multiple cDNAs are conducted in **one step**.

The distinction between the claimed invention and the methods disclosed in the Richardson *et al.* publication is critical. While the present invention shares with the known procedure the use of

a randomer sequence, so that the use of appropriate populations of varied FAP-RAND sequences gives multiple cDNAs, Applicants' claimed procedure is much simpler. Moreover, the reverse transcription proceeds more efficiently, and fewer amplification cycles are required.

Further, by comparison with the procedure in the Richardson *et al.* publication, the need for rare restriction sites is avoided. Another advantage is that the production of complex products is minimized, due in part to the use of unique sequences in the heeled 5'-amplification and the heeled 3'-amplification primers which are absent from the genome being investigated. Moreover, while the procedure described in the Richardson *et al.* publication uses a single primer to amplify the products after reverse transcriptase and second strand synthesis, the present invention provides the significant advantage that two separate primers of unique sequence are used.

Applicants' claimed invention not only provides greater amplification but also greater flexibility in use. For example, it readily allows the inclusion of specific restriction sites, for manufacturing subtracted normalized and enriched cDNA libraries. It also allows the inclusion of specific restriction sites for lambda cloning, for the manufacture of single cell libraries. Again, specific restriction sites can be included, for fragmentation, for use as probes on the microarrays and filters.

In view of the above, Applicants respectfully assert that the cited references do not teach or suggest each and every element of Applicants' claimed invention. As the Examiner is aware, in order to anticipate, a single reference must disclose within the four corners of the document each and every element and limitation contained in the rejected claim. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991). In regard to the obviousness rejection, the secondary reference fails to cure the deficiencies of the Richardson *et al.* publication. Accordingly, Applicants respectfully assert that the cited references do not anticipate or render obvious the claimed invention. Reconsideration and withdrawal of the rejections under 35 USC §102 and 35 USC §103 is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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